

CLAIMS

1. Use of anti-idiotypic antibodies of fibroblast growth factor 1, for the preparation of a medicament intended for treating diseases in which endothelial cells are involved in a process of angiogenesis, either to inhibit angiogenesis, or to promote angiogenesis, without affecting the quiescent endothelial cells, or for the preparation of a diagnostic product for diseases in which endothelial cells are involved in a process of angiogenesis.

2. Use of anti-idiotypic antibodies of fibroblast growth factor 1 according to Claim 1, for the preparation of a medicament intended for the treatment of diseases involving angiogenic endothelial cells, by selective stimulation of the FGFR-2b receptor.

3. Use of anti-idiotypic antibodies of fibroblast growth factor 1 according to one of the Claims 1 or 2, for the preparation of a medicament intended for the treatment of diseases in which endothelial cells are involved in a process of angiogenesis, for inhibiting angiogenesis, without affecting the quiescent endothelial cells, the said anti-idiotypic antibody being coupled to a toxin whose function is to block the translation of the proteins, the said toxin being selected in particular from saporin, ricin or a radioactive element such as iodine 125 or 131, or the said anti-idiotypic antibody being in the form of an Fab fragment.

4. Use of anti-idiotypic antibodies of fibroblast growth factor 1 according to one of the Claims 1 or 2, for the preparation of a medicament intended for the treatment of diseases in which endothelial cells are involved in a process of angiogenesis for promoting angiogenesis, without affecting the quiescent endothelial cells.

5. Use of anti-idiotypic antibodies of fibroblast growth factor 1 according to any one of the Claims 1, 2 or 4, for the preparation of a medicament intended for:

— promoting physiological angiogenesis for increasing the rate of formation of blood vessels during healing, or maturation of the corpus luteum of the ovary, and/or

– promoting angiogenesis in the course of obstructive diseases of vessels in order to reperfuse ischaemic regions in vascular thrombosis, especially in lower limb arteritis and myocardial infarction, and/or

– selectively stimulating the activity of the receptors of FGF1 in diseases in which the said receptors are functionally deficient, and/or

– selectively inhibiting the activity of the receptors of FGF1 by means of Fab fragments or of blocking anti-idiotypic antibodies, and/or

– delaying or stopping the process of degeneration of the photoreceptors of the neuroretina observed in pigmentary retinitis, either genetic or acquired during overdose of medicaments inhibiting cyclic-GMP-dependent phosphodiesterase, and/or

– stimulating phagocytosis of the external segments of the rods by the pigmented epithelial cells of the retina as treatment for certain pigmentary retinopathies and of dry forms of age-related macular degeneration.

6. Use of anti-idiotypic antibodies of fibroblast growth factor 1 according to any one of the Claims 1 to 3, combined with a toxin or Fab fragment of anti-idiotypic antibody, for the preparation of a medicament intended for the treatment of diseases requiring inhibition of angiogenesis, such as cancer, diabetic retinopathies and rejection of corneal grafts.

7. An anti-idiotypic antibody, especially monoclonal, and especially humanized, of fibroblast growth factor 1, characterized in that it is respectively a ligand of the human receptor FGFR-2b.

8. An anti-idiotypic antibody according to Claim 7, characterized in that it has the following properties:

- it is specific with respect to the FGFR-2b receptor,
- it is circulating,
- it has a half-life of about 23 days, especially of about 21 days, and in particular of 22.5 days,
- it induces the phosphorylation of a 140 kDa protein on a tyrosine,
- it induces the proliferation of vascular endothelial cells,
- it stimulates angiogenesis,
- it does not cause arterial hypotension.

sub 3

9. Fab fragment of an anti-idiotypic antibody according to Claim 7 or Claim 8.

10. A complex between an anti-idiotypic antibody according to Claim 7 or Claim 8 and a toxin, selected in particular from saporin, ricin, or alternatively a radioactive element such as iodine 125 or 131, or strontium.

sub 3

11. A method of preparation of an anti-idiotypic antibody of fibroblast growth factor 1 according to Claim 7 or Claim 8, characterized in that:

a) an animal, especially a rabbit, is injected with purified fibroblast growth factor 1 (FGF1),

b) blood is taken for recovering the purified immunoglobulins Ig containing specific anti-FGF1 antibodies (Ig1 F1), for example by protein-A affinity chromatography, then the specific Ig1 F1 are purified if necessary from the purified Ig's, for example by FGF1-affinity chromatography,

c) the aforesaid purified Ig's or the aforesaid specific, purified Ig1 F1's are injected into an animal of the same species as used for injection of FGF1, especially in the popliteal ganglia of a rabbit of the same allotype as that which produced Ig1 F1, during injection of FGF1,

d) blood is taken for recovering the total Ig's, for example by protein A, and then submitting the total Ig's to two immunoadsorptions:

– an immunoadsorption of an affinity column prepared with the pre-immune Ig's of the rabbit (Ig PI) that was used for making the Ig1 F1's, to eliminate the anti-allotypic or isotypic antibodies,

– an immunoadsorption on an affinity column prepared with the Ig1 F1's, to purify the anti-idiotypic antibodies (Ig2Id F1).

12. A method of preparation of a monoclonal anti-idiotypic antibody of FGF1 according to Claim 7 or Claim 8, characterized in that:

a) FGF1 is injected into an animal and especially a mouse,

b) the splenocytes are recovered from the animal synthesizing Ig1 F1's,

c) the aforesaid splenocytes are fused with myeloma cells,

d) the hybridomas obtained at the end of the preceding step c) are selected on the basis that they synthesize immunoglobulins directed against FGF1,

e) the Ig1 F1's thus selected at the end of step d) are injected into an animal, and especially a mouse, of the same allotype as that which produced Ig1 F1,

f) the splenocytes synthesizing Ig2Id F1's are recovered,

g) the cells from the spleen (splenocytes) are fused with myeloma cells,

h) the hybridomas obtained at the end of the preceding step g) are selected on the basis that they synthesize Ig2Id F1's directed against Ig1 F1,

i) the said Ig2Id F1's are recovered.

13. Pharmaceutical compositions, characterized in that they contain, as active substance, at least one anti-idiotypic antibody according to Claim 7 or Claim 8, or at least the Fab fragment according to Claim 9 or at least the complex according to Claim 10, in conjunction with a pharmaceutically acceptable vehicle.

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